Korennoy, F. I., Gulenkin, V. M., Gogin, A. E., Vergne, T. and Karaulov, A. K. (2016), Estimating the Basic Reproductive Number for African Swine Fever Using the Ukrainian Historical Epidemic of 1977. Transbound Emerg Dis. doi:10.1111/tbed.12583

TITLE: Estimating the Basic Reproductive Number for African Swine Fever Using the Ukrainian Historical Epidemic of 1977

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JOURNAL TITLE: Transboundary and Emerging Diseases

PUBLISHER: Wiley

PUBLICATION DATE: September 2016

DOI: 10.1111/tbed.12583

Estimating the basic reproductive number for African swine fever using the Ukrainian historical epidemic of 1977

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Abstract

In 1977, Ukraine experienced a local epidemic of African swine fever (ASF) in the Odessa region. A total of 20 settlements were affected during the course of the epidemic, including both large farms and backyard households. Thanks to timely interventions, the virus circulation was successfully eradicated within six months, leading to no additional outbreaks. Detailed report of the outbreak's investigation has become publically available in 2014. The report contains some quantitative data that allow studying the ASF spread dynamics in the course of the epidemic.

In our study, we used this historical epidemic to estimate the basic reproductive number of the ASF virus both within and between farms. The basic reproductive number (R_0) represents the average number of secondary infections caused by one infectious unit during its infectious period in a susceptible population. Calculations were made under assumption of an exponential initial growth by fitting the approximating curve to the initial segments of the epidemic curves. The within- and between-farm R_0 were estimated at 7.46 (95% confidence interval: 5.68 – 9.21) and 1.65 (1.42 – 1.88) respectively. Corresponding daily transmission rates were estimated at 1.07 (0.81 – 1.32) and 0.09 (0.07 – 0.10). These estimations based on historical data are consistent with those using data generated by the recent epidemic currently affecting Eastern Europe. Such results contribute to the published knowledge on the ASF transmission dynamics under natural conditions and could be used to model and predict the spread of ASF in affected and non-affected regions and to evaluate the effectiveness of different control measures.

Keywords: African swine fever, Ukraine, basic reproductive number, exponential initial growth, transmission rate.

Introduction

African swine fever is a viral contagious disease of domestic pigs and wild boar, which can be transmitted by direct contacts of susceptible animals with infectious ones or their tissues. Other possible routes of infection are: consumption of feed and swill contaminated by the virus and vector-borne transmission by soft ticks. Acute forms of the disease demonstrate a nearly 100 percent mortality in infected animals, although chronic and subclinical forms may be observed in regions where the disease is endemic (Morilla et al., 2002; Blome et al., 2012; Gallardo et al., 2015; Guinat et al., 2016). In the absence of an effective vaccine, the only effective control measures to prevent virus spread is the enforcement of strict movement restrictions of pigs, pig products and humans in affected areas and the culling of affected herds. Both measures incur severe economic losses to the pig industry (Costard et al., 2009).

Numerous observations of real-life outbreaks reveal that when introduced into a farm the virus not only spreads rapidly within the farm but is also transmitted to neighboring farms and backyard holdings. This short-distance transmission occurs mainly because of movements of pigs, pig products, waste and vehicles contaminated by the virus. Wild boar populations are also able to maintain circulation of the virus, making possible the virus introduction into pig farms by direct or indirect contact with wild boar; note that this transmission route might happen mostly in low biosecurity farms (Oganesyan et al., 2013; Vergne et al., 2015, 2016; Guinat et al., 2016).

In 1977, an ASF epidemic occurred in Odessa city (Ukraine, formerly the Ukrainian Soviet Socialist Republic of the USSR) and the neighboring settlements. ASFV was probably introduced by merchant vessels entering the Odessa seaport. Within 6 months the disease spread to 20 settlements located up to 200 km from Odessa city (Fig. 1). The virus was detected both in small scale backyard holdings and large pig farms. No signs of infection were found in wild boars during monitoring within areas adjacent to the infected settlements. Due to strict control measures based on stamping-out policies, the epidemic was eradicated and further spread of the virus prevented. A detailed report on the study of the outbreak and control measures aimed at its eradication has recently been published by the National Research Institute for Veterinary Virology and Microbiology (Russia), which was responsible for investigation of the epidemic in 1977 (Anonymous, 2014). The report contains, in particular, quantitative data that reflect the infection dynamics of the virus at farm level during the course of epidemic as well as pig mortality dynamics within the very first affected farm. The information at hand allows the estimation of the basic reproductive number (R_0), which is one of the main quantitative characteristics of an epidemic (Anderson and May, 1992). The basic reproductive number is the number of secondary disease cases one infected case is expected to cause in a susceptible population during its infectious period. It is widely used in quantitative epidemiology to characterize epidemic dynamics and evaluate control strategies.

This paper aims at estimating R_0 both within farms (when the virus is transmitted from infectious to susceptible animals) and between farms (when the virus is transmitted from infectious to susceptible farms).

Materials and methods

Data

This study was based on several incidence data recorded during the ASF epidemic in the Odessa Oblast of Ukraine during the period from February 10 to July 2, 1977 as reported in (Anonymous, 2014).

In the course of the epidemic, all samples were collected in affected holdings by regional veterinarians and forwarded to the National Research Institute for Veterinary Virology and

Microbiology, which possessed the only specialized ASF diagnostic laboratory in the USSR at the time of the event. The ASF was diagnosed by haemadsorption test (HAT) on porcine bone marrow cells, which is the OIE reference method of the ASF virus diagnostics (OIE, 2016). It was found that the ASF virus belongs to the genotype I serogroup 4, which was also responsible for epidemics in some European and South-American countries in 1964 – 1984 (Malogolovkin et al., 2015).

Two datasets are available in the report. The first one represents the observed dynamic of pig mortality at subsidiary farm in Usatovo village, which was the very first affected holding (see Annex, Table 1). We used these data in order to estimate the within-farm R_0. The second dataset contains observed incidence of the disease at farm level (see Annex, Table 2). This information includes the disease onset date, the final diagnosis date and the number of susceptible animals in each of the 20 affected locations in the Odessa oblast. These data were used for estimation of between-farm R_0. The name and level of administrative division were also recorded for each settlement enabling their geographical location to be established and mapped.

Overview of the method used to estimate R_0

In order to estimate R_0 both within and between farms, we used the method of initial exponential growth based on the analysis of the initial segment of the epidemic curves. This method assumes that, in a homogeneously mixed population of susceptible units (either pigs within a farm and farms within the study area), the number of new cases increases exponentially during the initial stages of the epidemic. According to (Iglesias et al., 2011), R_0 can be defined as:

$$R_0 = 1 + \frac{D * ln(N_t / N_0)}{t} \qquad (1),$$

where D is the duration of infectious period, i.e. the period during which an infected animal (or an infected farm) can infect susceptible animals (or susceptible farms); N_t and N_0 are numbers of newly infected animals (or farms) at the time t and at the beginning of the epidemic, respectively. In general, t is set at the time it takes for the incidence to double i.e. the time at which $N_t = 2 \times N_0$(Dietz, 1993; Zhang et al., 2012). Since the duration of infectious period D cannot be measured or estimated directly, we used three values coming from the literature as three scenarios.

From the estimation of R_0, we calculated the transmission rate β which, in our case, represents the daily rate at which infectious animals (or farms) infect susceptible ones. It was calculated as follows:

$$\beta = R_0/\mathrm{D} \qquad (2).$$

Estimation of R_0 between farms

1. For each of 20 affected farms, we measured the time spent between the disease onset and the final diagnosis - D_{bf}. Once the ASF has been recognized in the region, in some cases clinical diagnostics took place with subsequent laboratory confirmation by HAT, which resulted in very short D_{bf} of 2 – 3 days. An arithmetic mean value $\overline{D}_{bf}$ equal to 19 days was accepted as a median scenario of a farm's infectious period, and used as a time step for epidemic curve. This reflects our assumption that a farm could remain infectious until ASF is diagnosed and all pigs depopulated. Even though in many cases a holding was quarantined before the ASF confirmation, it has been reported that the transmission of the virus could have happened even after quarantine being imposed (Anonymous, 2014). To reflect the uncertainty on this parameter, two other values of a farm's infectious period were taken from literature: 15 days (Gulenkin et al., 2011) and 30 days (Barongo et al., 2015).
2. The entire period from February 10 to July 2, 1977 was divided into equal periods of duration $\overline{D}_{bf}$; the number of newly infected holdings N_t was calculated for each period, which resulted in construction of the epidemic curve.

3. An exponential model was fitted to the observed incidence during the initial stage of the epidemic, i.e. from the onset of the epidemic to its peak (Fig. 2). Goodness of a model fit was assessed by means of R-squared value, which represents the percentage of the dependent variable's variation explained by the independent variable.
4. The mean and the confidence interval of the estimated parameter driving the exponential growth were used to estimate R_{0bf} using formula (1). The calculations were performed using Monte Carlo simulation with 10,000 iterations. The median value of R_0 and the 95% confidence interval limits were established for each of the three D scenarios.
5. We estimated the transmission rate β_{bf} and its confidence interval using formula (2).

Estimation of R0 at the on-farm level

1. According to subsequent experiments with the ASF virus strain that caused the epidemic in Odessa region, the duration of the infectious period in pigs infected by direct contact (group housing) was between 3 and 14 days (Anonymous, 2014). Similar values were also used by Guinat et al., 2015. We accepted these values as boundary scenarios, while 7 days was taken as a median scenario being a mean typical infectious period of ASF in pigs (D_{wf}) used in literature (Table 1).
2. Three epidemic waves were observed in the course of epidemics in the study farm, which could be due to animals being kept in different buildings of the farm. Assuming that the force of infection between animals of different buildings was negligible as compared to the force of infection between animals of the same building, the three waves (February 11-13, 15-19 and 20-23) were considered independent for the analysis. In a similar way to the between-farm study, we fitted three exponential models to the three observed

incident curves for three time periods (Fig. 3) and estimated the means and the 95% confidence intervals of the basic reproductive numbers R_{0wf} and of the transmission rate β_{wf} for each of the three epidemic waves.

3. We used the bootstrap technique for random sampling from the three acquired distributions in order to estimate the median value of R_{0wf} for the infectious period equal to 7 days, which considered a most typical scenario.

Table 1. Summary of modelling studies estimating transmission parameters of ASFV in domestic pigs (see also Guinat et al., 2016)

Study	Genotype	Virus isolate	Duration of infectious period, days	Between-farm R_0	Within-farm R_0
Belyanin et al., 2011	II	various	6.8 (5.0 – 8.6)	-	-
De Carvalho Ferreira at el., 2013	I	Malta’78 Netherlands’86	6.8±1.8 4.6±1.4	-	18.0 (6.90 – 46.9) 4.92 (1.45 – 16.6)
Pietschmann et al., 2015	II	Armenia’08	2 - 9	-	6.1 (0.6 – 14.5) 5.0 (1.4 – 10.7)
Guinat et al., 2015	II	Georgia 2007/1	3 - 14	-	5.0 (2.4 – 9.1) within pen 2.7 (0.7 – 5.2) between pen
Gulenkin et al., 2011	II	Stavropol 01/08	5 within farm 15 between farm	2 - 3	8 - 11
Barongo et al., 2014	IX	Uganda	30 between farm	3.24 (3.21 – 3.27) 1.63 (1.6 – 1.72)	-

				1.90 (1.87 – 1.94) 1.58 1.77 (1.74 – 1.81)	
Current study	I	O-77	7 within farm 19 between farm	1.65 (1.42 – 1.88)	7.46 (5.68 – 9.21)

Software

The standard Microsoft Office Excel 2003 package (Microsoft, USA) with @Risk 4.5 add-on (Palisade, USA) was used for data processing, distribution fitting and for Monte-Carlo simulations. Exponential models' fitting was performed in R statistical software environment (R Core Team, 2014). ArcGIS 10.3.1 (Esri, USA), a GIS software system, was used for georeference and geovisualization.

Results

The estimates of basic reproduction numbers and transmission rates for different scenarios of between-farm and within-farm ASFV spread are presented in Tables 2 and 3 together with corresponding values of R-squared used to asses goodness of models' fit. For an infectious period duration of 19 days in affected farms, the between-farm R_0 was estimated at 1.65 (95%CI: 1.42 – 1.88), leading to a daily transmission rate between farms of 0.09 (0.07 – 0.10). For an infectious period duration of seven days in pigs, averaged within-farm basic reproduction number and daily transmission rate were estimated at 7.46 (5.68 – 9.21) and 1.07 (0.81 – 1.32), respectively. It should be noted for both between- and within farm transmission, that while the estimations of the daily transmission rate were relatively consistent across the different scenarios of infectious period duration, the estimations of the basic reproduction number varied greatly.

Table 2. Estimated values of basic reproductive numbers and transmission rates at between-farm level

	D_{bf}, days		
	15	19	30
R_{0bf}	1.51 (1.33 – 1.70)	1.65 (1.42 – 1.88)	2.03 (1.66 – 2.39)
β	0.10 (0.09 – 0.11)	0.09 (0.07 – 0.10)	0.07 (0.06 – 0.08)
R-squared	0,9098		

Table 3. Estimated values of basic reproductive numbers and transmission rates at within-farm level

	1st wave			2nd wave			3rd wave		
D_{wf}, days	3	7	14	3	7	14	3	7	14
R_{0wf}	3.35 (2.88 – 3.82)	6.49 (5.41 – 7.57)	11.98 (9.77 – 14.18)	3.97 (3.43 – 4.50)	7.93 (6.64 – 9.21)	14.87 (12.28 – 17.46)	3.98 (3.37 – 4.59)	7.97 (6.49 – 9.38)	14.91 (12.07 – 17.80)
β	1.12 (0.96 – 1.27)	0.93 (0.77 – 1.08)	0.86 (0.70 – 1.01)	1.32 (1.14 – 1.50)	1.13 (0.95 – 1.32)	1.06 (0.88 – 1.25)	1.33 (1.12 – 1.53)	1.14 (0.93 – 1.34)	1.07 (0.86 – 1.27)

R-squared	0.9799	0.9741	0.9675

Discussion

Quantitative data on the natural ASF epidemic spread dynamics, especially within an infected farm, can rarely be found in academic literature (Guinat et al., 2016), which is why this study is relevant not only in terms of the R_0 estimation but also in terms of the systematization and publication of the retrospective ASF outbreak data.

As shown in Table 1, the results of this study are in close agreement with the results obtained by other authors. It should be noted that the available data on the between-farm ASFV transmission were acquired by studying real-life outbreaks having occurred in different regions and countries of the world caused by different virus genotypes. Quantitative characteristics of between-farm ASFV transmission calculated by different authors are virtually identical. A lower dependence of the between-farm ASFV transmission rate on the biological properties of the virus can be assumed since such transmission is mainly facilitated by the livestock management structure, the intensity of business interactions between farms and by trade.

As for the within-farm transmission, the majority of published data are based on laboratory experiments in which different methods, doses and virus strains were used for animal inoculation, which is bound to influence the quantitative characteristic of the infectious period duration (see Table 1 and Guinat et al., 2016). This is why a huge variability is seen in the estimations of R_0. The study by Gulenkin et al., 2011 is the only published research to date in which the within-farm R_0 was estimated in field conditions presented by 3 ASF outbreaks on the territory of the Russian Federation.

The assumption of a homogenous mixing of the population under study implies that every susceptible unit in the population has an equal probability of becoming infected whichever unit is infectious. The country was unaware of the ASF in 1977 and no any disease-specific protective measures were applied even at large collective farms and state farms. It should be noted that 11 out of 20 affected farms, including the very first one used for the modeling, were represented by private backyards or subsidiary holdings that can be considered low biosecurity holdings easily exposed to the virus introduction. Within such farms, pigs were likely to be in close contact with each other, validating the assumption of homogeneous mixing at within-farm level. Also, despite that farm distribution is spatialized making transmissions theoretically more likely between farms that are close to each other, the relatively small scale of the affected region makes us believe that the assumption of homogeneous mixing of farms is acceptable and did not generate misleading results. This homogeneous mixing is indirectly supported by the fact that the initial growth of the incidence (both within and between farms) almost perfectly followed an exponential model (see Figures 2, 3 and R-squared values in Tables 2 and 3), which is the case under the homogenous mixing assumption. The estimation of R_{0bf} for the strain responsible for the ASF epidemic in the Odessa region in 1977 can help in understanding the spatiotemporal characteristics of the ongoing ASF epidemic in the European part of Russia and in Eastern European countries by simulating between-farm spread of the virus in case of introduction into a disease-free region. Given that there are no vaccines available which could be used for either emergency or preventive vaccination of pigs against ASF, one of the methods of containing the spread of the disease is stamping out of the susceptible animal population. Such a method is associated with the following problems: 1) the size of the risk zone of a possible disease spread from an initial outbreak area (farm, affected location) to other farms is unknown and should be estimated; 2) the minimal number of farms where depopulation is to be carried out should be estimated. Knowing the R_0 value for the transmission at the between-farm level the number of farms which are to be depopulated can be calculated using the following ratio: $p = 1 - 1/R_0$ (Anderson and May, 1992). We calculated *p* to be 0.39 (0.29-0.47) taking into account the previously established median R_{0bf} value. Consequently, we can state that in order to guarantee the prevention of an epidemic in the region where ASFV has been introduced, the susceptible population on at least 29% of pig farms theoretically should be stamped out. During the epidemic in Odessa region, 30.5% of susceptible pig population of the whole region (the area of which amounts to ~33,000 km^2) was depopulated, while 100% of pigs were depopulated within 5 to 20 km zone of an approximate total area up to 8,000 km^2 around infected holdings (Fig. 1), which allowed prevention of the virus circulation in the region (Anonymous, 2014). Based on these measures, a new edition of the Instruction on Prevention and Eradication of ASF (Anonymous, 1980), which is currently in use in the Russian Federation, was accepted. It requires that a protective zone of 5 – 20 km radius should be applied around an infected holding. Total depopulation of susceptible pigs must be enforced within this zone. Additionally, a surveillance zone 100 - 150 kilometers in radius, where enhanced monitoring measures and restrictions on animal movement and trade of live pigs and pig products are put in place, should be established. In comparison, current EU legislation requires total stamping-out within an infected holding only. Protection and surveillance zones of 3 km and 10 km in radius respectively should be established with enhanced screening and pigs' movement prohibition within 30 days after ASF confirmation (Council Directive, 2002). These requirements are consistent with the measures applied during eradication of the ASF in Spain 1985 – 1995 (Morilla et al., 2002). Apparently, regulations of Russian Instruction are significantly stricter, but their effective implementation may be difficult. Indeed, it has been shown that the ASF virus can spread to a distance of more than 100 kilometers from an initial outbreak area (Korennoy et al., 2014; Iglesias et al., 2015), that underlines a significance of further studies on between-farm ASFV spread patterns. The development of spatially-explicit between-farm transmission models is attractive but would be hampered by the lack of data on the population at risk, particularly regarding the location of all farms in the region and the number of pigs kept in each.

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Figure 1. Study area and the ASF infected holdings. Numeration is consistent with Table 2 (see Annex).

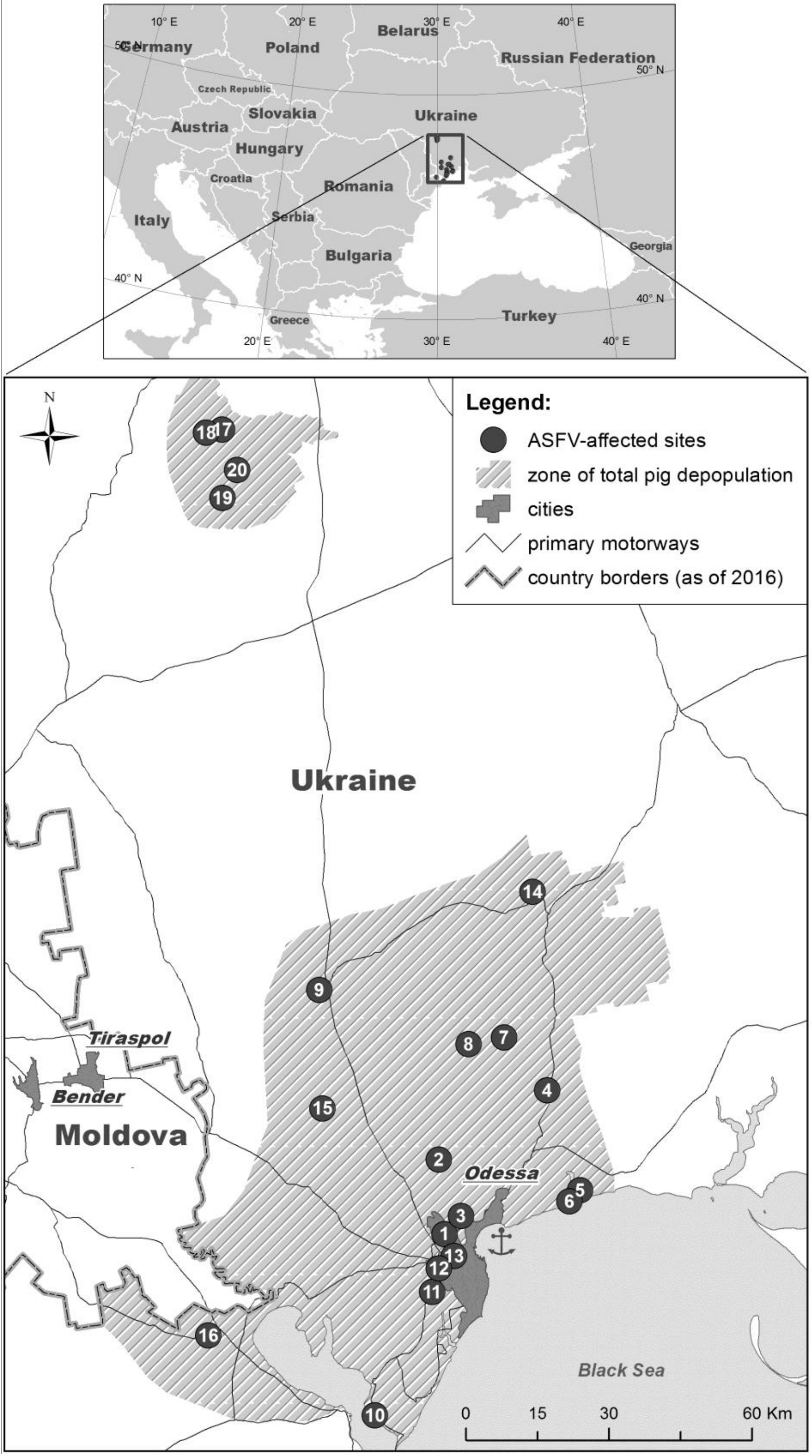

10° E
20° E
30° E
40° E
50° N
Germany
Poland
Belarus
Russian Federation
50° N
Czech Republic
Slovakia
Ukraine
Austria
Hungary
Croatia
Romania
Italy
Serbia
Bulgaria
Georgia
40° N
Greece
Turkey
40° N
20° E
30° E
40° E
N
Legend:
● ASFV-affected sites
▨ zone of total pig depopulation
cities
primary motorways
country borders (as of 2016)
18
17
20
19
Ukraine
14
9
8
7
4
15
2
Odessa
5
6
3
1
13
12
11
16
10
Tiraspol
Bender
Moldova
Black Sea
0
15
30
60 Km

Figure 2. Dynamics of the epidemic process on the between-farm level and fitted exponential model with standard deviations

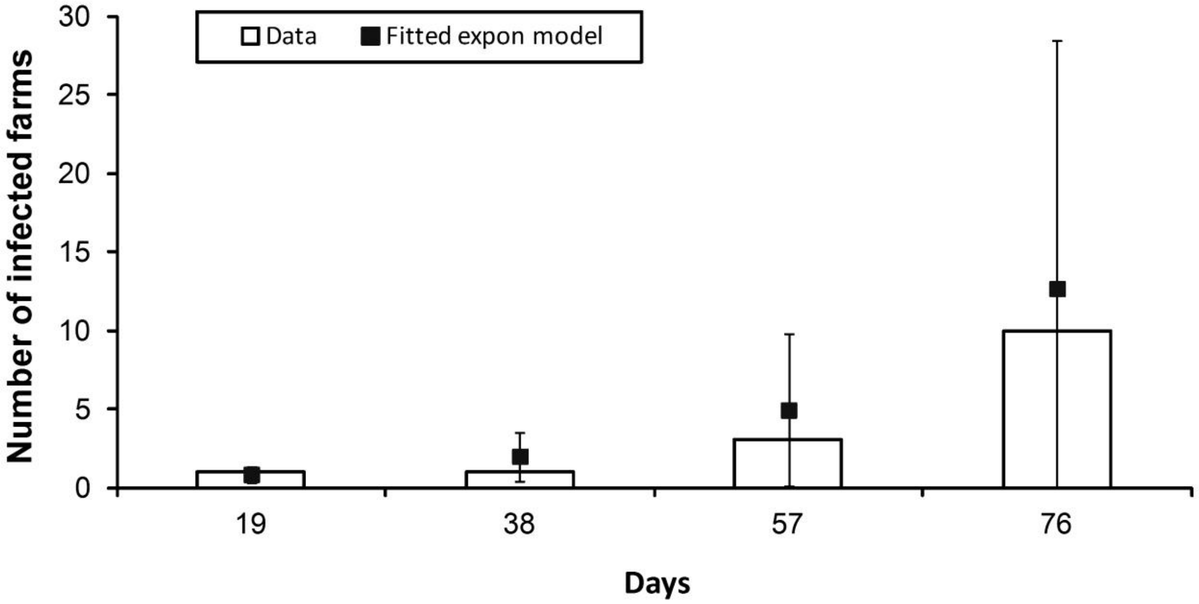
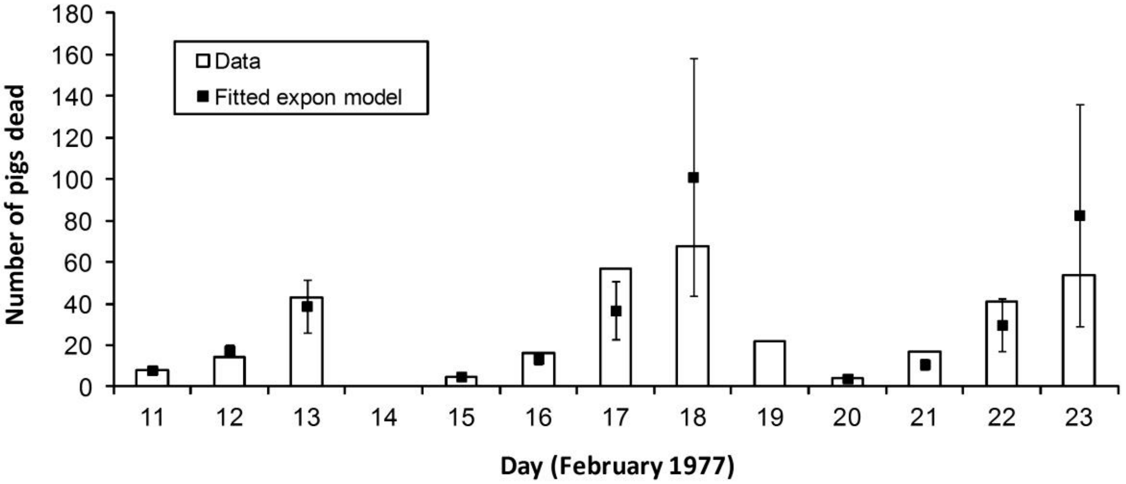


Figure 3. Dynamics of disease detection on a farm in Usatovo village and fitted exponential models with standard deviations



Annex

Table 1. Dynamics of diseased animal detection on a farm in Usatovo village (adopted from Anon., 2014)

Date	Number of clinical cases in animals
11.02.1977	8
12.02.1977	14
13.02.1977	43
15.02 – 16.02.1977	21
17.02.1977	57
18.02.1977	68
19.02.1977	22
20.02.1977	4
21.02.1977	17
22.02.1977	41
23.02.1977	54

Table 2. Affected holdings recorded in the period from February to July 1977 (adopted from Anon., 2014)

Raion	Num on map	Name of location, holding	Number of susceptible animals	Date of disease occurrence	Date of final diagnosis

(2-level administrative divisions)					
Belyaevsky	1	Usatovo village, subsidiary holding	4746	10.02.1977	11.04.1977
	2	Ilinka, ‘Chapaeva’ collective farm	3659	13.04.1977	20.04.1977
	3	Naberezhny village, subsidiary holding of a military base	105	15.04.1977	20.04.1977
Kominternovsky	4	Kominternovskoe village, ‘XX Partsyezda’ collective farm	7585	19.03.1977	05.04.1977
	5	Belyari village, ‘Udarnik’ subsidiary holding	1330	05.04.1977	11.04.1977
	6	Grigorovka village, subsidiary holding of a military base	57	10.04.1977	20.04.1977
	7	Oniskovo village, fattening state farm	2298	08.04.1977	20.04.1977

Ivanovsky	8	Buyalik village, subsidiary holding of a military base	79	04.04.1977	11.04.1977
	9	Krasnoznamenka village, ‘Druzhba narodov’ collective farm	12582	11.04.1977	20.04.1977
Ovidiopolsky	10	Roksolyany village, ‘Lenina’ collective farm	2627	17.04.1977	20.04.1977
	11	Prilimanskoe village, private backyard holding	6	05.04.1977	20.04.1977
Odessa city	12	Lenposelok village, subsidiary holding of a military base	52	16.04.1977	20.04.1977
	13	Krivaya Balka village, private backyard holding	21	09.04.1977	20.04.1977
Berezonsky	14	Berezovka town, private backyard holding	2	21.04.1977	23.04.1977

Razdelnyansky	15	Novodmitrievka village, ‘Shlyakhom Lenina’ collective farm	13865	12.04.1977	06.05.1977
Belgorod Dnestrovsky	16	Starokozachye village, ‘XXI Partsyezda’ collective farm	11372	20.05.1977	25.05.1977
Savransy	17	Osichki village, ‘Druzhba’ collective farm	1834	27.05.1977	02.07.1977
	18	Kantseba village, private backyard holding	18	19.05.1977	08.07.1977
	19	Belousovka village, Kotovskogo collective farm	1509	19.05.1977	29.07.1977
	20	Nedelkovo village, private backyard holding	3	02.07.1977	19.07.1977